Amendments to the Specification:

Please replace the paragraph which begins on page 4, line 15 of the specification with the following amended paragraph:

FT-IR microscopic determination of collagen orientation in articular cartilage was discussed in Camacho, N.P., Mendelsohn, R., Grigiene, R., Torzilla, P.A., "Polarized FI-IR Microscopic Determination of Collagen Orientation in Articular Cartilage", 42nd Annual Meeting, Orthopaedic Research Society, February 19-22, 1996, Atlanta, Georgia. FT-IR microscopic imaging of the major components of articular cartilage was discussed in "FT-IR Microscopic Imaging of Collagen and Proteoglycan in Bovine Cartilage", Camacho, N.P.; West, P.; Torzilli, P.A.; Mendelsohn, R., Biopolymers, 62:1-8 (2001). FT-IR microscopic imaging analysis of bovine nasal cartilage components utilizing multivariate analysis was discussed in Potter, K., Kidder, L.H., Levin, I.W., Lewis E.N., Spencer R.G., Arthritis & Rheum, 44(4):846-[[55]] 855 (2001).

Please replace the paragraph bridging pages 19 and 20 with the following amended paragraph:

All imaging data were analyzed in WinIR Pro software (Bio-Rad). The areas of the amide I and II absorbances and the proteoglycan absorbances were calculated for each spectrum between 1710-1595, 1595-1510, and 960-1185 cm^{-1}, respectively.

C2

Infrared images were then created based on these absorbances. For the polarization data, it was assumed that the amide I absorbance arises primarily from the C=O (carbonyl) stretching vibration of the type II collagen and was oriented approximately perpendicular to the collagen fibril long axis. Since the amide I and amide II absorbances have inverse polarizations (Gadaleta, S.J., Landis, W.J., Boskey, A.L., and Mendelsohn, R., "Polarized FT-IR Microscopy of Calcified Turkey Leg Tendon", Connect. Tissue Res., 34, pp. [[230]] 203-211, (1996)), the ratio of the areas of amide I: amide II absorbances in one polarization (perpendicular to the articular surface) was calculated and imaged as an indicator of orientation. For this case, a larger amide I:amide II ratio represents collagen fibrils oriented parallel to the cartilage articular surface. The total area of the amide I plus amide II was imaged to show the collagen distribution in the polarized sections.

Please replace the last paragraph on page 20 with the following amended paragraph:

G3

FT-IRM (Fig. 1B) spectra were obtained from the superficial, mid and deep zones of articular cartilage sections (Fig. 1A). Comparison to spectra from the model compounds type II collagen, aggrecan, and water (Fig. 2) was necessary to interpret the absorbances. The primary absorbances attributed to collagen molecules arise from the following carbonyl group containing compounds: Amide A, I, II and III (Table I).

Please replace the second paragraph on page 22 with the following paragraph:

G4

Since the spectra of isolated type II collagen and aggrecan displayed considerable overlap, it was necessary to analyze mixtures of these two compounds to determine the best way to quantitate the individual components in cartilage ([[Fig.]] Figs. 3A to 3G). Upon increasing the ratio of aggrecan to collagen, several successive changes were noted in the spectra of the collagen-aggrecan mixtures. The primary changes that were

potentially suitable as quantitative indicators were the shift in the amide I and amide II absorbances from approximately 1660 to 1643 cm^{-1} (Fig. 3B) and approximately 1553 to 1564 cm^{-1} (Fig. 3C) and the integrated areas of the 960-1185 cm^{-1} (Fig. 3D)and the 830-880 cm^{-1} (Fig.3E) absorbance regions. It was also determined that the areas of the amide I band (1710-1595 cm^{-1}) (Fig. 3F) and the absorbance centered at 1338 cm^{-1} (Fig. 3G) were directly correlated to the quantity of type II collagen in the mixtures.

A4

Please replace the following paragraph on page 23, which begins on line 12, with the following amended paragraph:

A5

Polarized FT-IRM spectra from the superficial (Fig. 6A) and deep zones (Fig. 6B) of cartilage showed different intensities of the collagen absorbances, particularly the amide I and II bands, indicative of changes in average orientation of the collagen molecules~~(Fig. 6)~~. The spectra from the midzone did not show any obvious polarization. FT-IRI was utilized to image the orientation of the collagen fibrils based on the amide I:amide II ratio (Fig. 7[[A]]<u>B</u>). With this technique, the zonal differences in orientation were readily apparent. The collagen fibril

orientation changed gradually from parallel to the articular surface in the superficial zone, to perpendicular to the articular surface in the deep zone.

A5

Please replace the paragraph bridging pages 26 and 27 with the following amended paragraph:

A6

The amide I region of collagen has three primary underlying components that contribute to the broad absorbance contour. Recently, studies have linked changes in the areas of these components to changes in integrity and possibly cross-links of the collagen fibrils (Pachalis, E.P., F. ~~Bets~~ Betts, E. DiCarlo, J.M. Lane, R. Mendelsohn, and A.L. Boskey, (1997), "Mineral and Organic Matrix Changes in Osteoporosis", J. Dent. Res., 76, p. 287; M. Khan, M. Yamauchi, S. Srisawasdi, D. Stiner, S. Doty, E.P. Paschalis, A. L. Boskey, (2001), "Homocysteine Decreases Chondrocyte-Mediated Matrix Mineralization in Differentiating Chick Limb-bud Mesenchymal Cell Micro-Mass Cultures", Bone, in press). A similar protocol will be utilized in the current study to evaluate the integrity of the type II collagen fibrils in cartilage. This data will be compared to immunohistochemical data

sensitive to damaged type II collagen fibrils (Hollander, A.P., T.F. Heathfield, C. Webber, Y. Iwata, R. Bourne, C. Rorabeck, and A.R. Poole, (1994), "Increased Damage to Type II Collagen in Osteoarthritic Articular Cartilage Detected by a New Immunoassay", Journal of Clinical Investigation, 93, pp. 1722- ~~2732~~ 1732).

G6 Cont.